REMARKS

This application has been amended in a manner that is believed to place the application in condition for allowance at the time of the next Official Action.

Claims 1-42 are canceled. New claims 43-62 have been added. Support for claims 43-62 may be found generally throughout the specification and in claims 1-42. Applicants respectfully submit that no new matter has been added.

Claims 4, 6-14, 16-25 and 39-40 were rejected under 35 U.S.C. §102(b), allegedly being anticipated by Heinicke et al., US 5,834,024. This rejection is respectfully traversed.

Heinicke *et al* disclose (see column 2, lines 23 to 40) a controlled absorption diltiazem pellet formulation comprising a mixture of long and short lag pellets. Each pellet has a core comprising diltiazem as the active ingredient. The core has a coating which is a single layer comprising a minor proportion of a pharmaceutically acceptable film-forming first polymer that is permeable to water and diltiazem and a major proportion of a pharmaceutically acceptable film-forming second polymer that is less permeable to water, and diltiazem than the first polymer. It is disclosed (see column 2, line 49 to 53) that the film forming polymers are preferably cationic polymers synthesised from acrylic and methacrylic acid esters with a low content of quaternary ammonium groups, such as Eudragit RL and Eudragit RS which are pH insensitive polymers.

In this regard, one skilled in the art would have appreciated that Heinicke *et al* is concerned exclusively with time-controlled release of diltiazem.

Heinicke *et al* also discloses (see column 5, lines 24 to 32) that time-controlled release may be achieved using a single coating layer alternatively comprised of a mixture of polymers, synthetic and/or naturally occurring, but are freely permeable, slightly permeable, i.e., water soluble or water insoluble polymers exhibiting a variety of properties.

Heinicke *et al* exemplifies a mixture of short and long lag pellets wherein each pellet consists of sugar spheres coated with a diltiazem coating to form the cores which are then divided into two parts, the first part being coating with a mixture of Eudragit RS and Eudragit RL and the second part being coated with a thicker coating of the same coating formulation.

However, there is no disclosure in Heinicke *et al* of coating the surface of pellets directly with a pH sensitive material as a film forming material for pH-mediated release of an active agent. This recitation is recited in each of independent Claims 43, 61, and 62. The remaining claims at issue are also novel over Heinicke *et al* by virtue of the dependency of these claims from new Claim 43, 61, and 62.

Claims 4, 6-14, 16-18, 25, 39 and 40 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Heinicke et al, US 5,834,024. This rejection is respectfully traversed.

Applicants respectfully submit that Heinicke et al fails to disclose or suggest a composition having of a pH sensitive coating material as a film forming material in direct contact with a rough, irregular surface of a pellet. In addition, there is no suggestion that coating a pellet in this way provide the pH controlled

release as observed with the present invention and described above. With this in mind, one skilled in the art would lack the motivation to modify Heinicke *et al* in a manner that would result in the claimed invention. Indeed, there is no suggestion in the publication that would prompt the skilled person to consider directly coating an uncoated pellet with a pH sensitive coating material to achieve the subtle pH controlled release observed in the present invention.

In view of the above, Applicants respectfully submit that Heinicke et al fails to disclose or suggest the claimed invention.

Claim 4, 6-18, 25 and 39-42 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Speirs in view of Andre et al. This rejection is respectfully traversed.

Speirs discloses a controlled release dosage form comprising enteric coated pellets of prednisolone metasulphobenzoate incorporated into an enteric coated capsule for use in the treatment of inflammatory bowel disease, especially ulcerative colitis and Crohns disease. Andre *et al* discloses a controlled release dosage form for producing at least a timed pulse involving rapid and complete controlled release of a pharmaceutical substance a fixed time after administration (see paragraph [001]). The composition comprises a delayed release coated core comprising an active substance and a polymer coating comprising at least one or more ammonio methacrylate copolymers, characterized in that the core comprises at least a surfactant. Suitable ammonio methacrylate materials include Eudragit RS and Eudragit RL (see paragraphs [001] and [0017]). It is disclosed (see paragraph [0025]) that, in certain embodiments, the dosage is one

that is formulated to obtain a timed pulse release independent of pH. Andre *et al* exemplifies non-pareil beads coated with a mixture of Eudragit RS and Eudragit RL.

However, neither Speirs nor Andre *et al* provides any suggestion that would prompt the skilled person to consider coating different pluralities of uncoated pellets with different thicknesses of a pH sensitive coating material for pH controlled release of an active. Furthermore, neither of these documents provides any suggestion that a composition comprising different pluralities of pellets coated in this way would have any effect on the rate of release of the active relative to pH, let alone increasing the release rate as the pH of the surrounding medium increases.

Accordingly, the proposed combination of Speirs in view of Andre *et al* fails to render obvious any of the claims.

In view of the above, applicants respectfully request that each of the rejections discussed above be withdrawn.

Applicants also submit herewith a PTO/SB/8a form ("IDS form") with the present Amendment. The form cites United States Patent No. 6,267,990 in the name of Fischer et al (" '990 patent"). As the Examiner is aware, the present application is a national stage application of International Patent Application No. PCT/GB2003/002911. The '990 patent was cited in the International Search Report issued in the International Patent Application, as shown in the Image File Wrapper for the above-identified application (see Patent Application Information Retrieval system, "2004-12-17 Documents Submitted with 371 Applications").

However, it appears that the Information Disclosure Statement filed on December 28, 2004 contained a typographical error identifying the '990 patent as United States Patent No. 6,267,994. Accordingly, Applicants respectfully request that the attached IDS form be completed to correctly show that the '990 patent has been considered. In that the '990 patent was already cited in the International Search Report, Applicants respectfully submit that no fee is due at this time. Nevertheless, if the Patent Office is of a different opinion, the Patent Office is authorized to charge the 37 C.F. R. 1.17(p) fee to Deposit Account No. 02-0200.

Conclusion

In view of the present Amendment and foregoing Remarks, therefore, applicants believe that the present application is condition for allowance at the time of the next Official Action. Accordingly, an early notification of allowance is earnestly solicited.

Respectfully submitted,

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APPENDIX

- PTO/SB/8a form